CLAIMS

1. A method for *in vivo* down-regulation of amyloid precursor protein (APP) or beta amyloid (Aβ) in an animal, the method comprising effecting presentation to the animal's immune system of an immunogenically effective amount of at least one analogue of APP or Aβ that incorporates into the same molecule a substantial fraction of B-cell epitopes of APP and/or Aβ so that the analogue reacts to the same extent as does APP or Aβ with a polyclonal serum raised against APP or Aβ, and at least one foreign T-helper epitope (T_H epitope) so that immunization of the animal with the analogue induces production of antibodies against the animal's autologous APP or Aβ, wherein the analogue

a) is a polyamino acid that contains the at least one foreign T_H epitope and a disrupted APP or Aβ sequence so that the analogue does not include any subsequence of SEQ ID NO: 2 that binds productively to MHC class II molecules initiating a T-cell response; and/or

b) is a conjugate comprising a polyhydroxypolymer backbone to which is separately coupled a polyamino acid as defined in a); and/or

c) is a conjugate comprising a polyhydroxypolymer backbone to which is separately coupled 1) the at least one foreign T_H epitope and 2) a disrupted sequence of APP or Aβ as defined in a).

2. The method according to claim 1, wherein the animal is a human being.

3. The method according to claim 1, wherein

- at least one first moiety is introduced which effects targeting of the analogue to an antigen presenting cell (APC) or a B-lymphocyte, and/or

- at least one second moiety is introduced which stimulates the immune system, and/or

- at least one third moiety is introduced which optimizes presentation of the analogue to the immune system.

4. The method according to claim 3, wherein the first and/or the second and/or the third moiety is/are attached as side groups by covalent or non-covalent binding to suitable chemical groups in the APP or Aβ sequence.

5. The method according to claim 1, wherein the analogue comprises a fusion polypeptide.

6. The method according to claim 1, wherein the analogue includes duplication of at least one B-cell epitope of APP or Aβ and/or introduction of a hapten.

7. The method according to claim 1, wherein the foreign T-cell epitope is immunodominant in the animal.

8. The method according to claim 1, wherein the foreign T-cell epitope is promiscuous.

9. The method according to claim 8, wherein the promiscuous foreign T-cell epitope is selected from a natural promiscuous T-cell epitope and an artificial MHC-II binding peptide sequence.

10. The method according to claim 8, wherein the natural T-cell epitope is selected from a Tetanus toxoid epitope, a diphtheria toxoid epitope, an influenza virus hemagluttinin epitope, and a *P. falciparum* CS epitope.

11. The method according to claim 10, wherein the Tetanus toxoid epitope is selected from P2 and P30.

12. The method according to claim 1, wherein the analogue comprises B-cell epitopes which are not exposed to the extracellular phase when present in a cell-bound form of the precursor polypeptide Aβ.

13. The method according to claim 1, wherein the analogue lacks at least one B-cell epitope which is exposed to the extracellular phase when present in a cell-bound form of the precursor polypeptide.

14. The method according to claim 1, wherein the analogue comprises at most 9 consecutive amino acids of SEQ ID NO: 2.

15. The method according to claim 14, wherein the analogue comprises at most 8 consecutive amino acids of SEQ ID NO: 2.

16. The method according to claim 14, wherein the analogue comprises at most 7 consecutive amino acids of SEQ ID NO: 2.

17. The method according to claim 14, wherein the analogue comprises at most 6 consecutive amino acids of SEQ ID NO: 2.

18. The method according to claim 14, wherein the analogue comprises at most 5 consecutive amino acids of SEQ ID NO: 2.

19. The method according to claim 14, wherein the analogue comprises at most 4 consecutive amino acids of SEQ ID NO: 2.

20. The method according to claim 14, wherein the analogue comprises at most 3 consecutive amino acids of SEQ ID NO: 2.

21. The method according to claim 14, wherein the analogue comprises at least one subsequence of SEQ ID NO: 2 so that each such at least one subsequence of SEQ ID NO: 2 independently consists of amino acid stretches selected from the group consisting of 9 consecutive amino acids of SEQ ID NO: 2, 8 consecutive amino acids of SEQ ID NO: 2, 7 consecutive amino acids of SEQ ID NO: 2, 6 consecutive amino acids of SEQ ID NO: 2, 5 consecutive amino acids of SEQ ID NO: 2, 4 consecutive amino acids of SEQ ID NO: 2, and 3 consecutive amino acids of SEQ ID NO: 2.

22. The method according to claim 14, wherein the consecutive amino acids begin at an amino acid residue selected from the group consisting of residue 672, 673, 674, 675, 676, 677, 678, 679, 680, 681, 682, 683, 684, 685, 686, 687, 688, 689, 690, 691, 692, 693, 694, 695, 696, 697, 698, 699, 700, 701, 702, 703, 704, 705, 706, 707, 708, 709, 710, 711, 712, 713, and 714.

23. The method according to claim 1, wherein presentation to the immune system is effected by having at least two copies of an Aβ derived fragment or the analogue covalently or non-covalently linked to a carrier molecule capable of effecting presentation of multiple copies of antigenic determinants.

24. The method according to claim 1, wherein the analogue is a conjugate comprising a polyhydroxypolymer backbone to which is separately coupled a polyamino acid that contains the at least one foreign T_H epitope and a disrupted APP or Aβ sequence so that the analogue does not include any subsequence of SEQ ID

NO: 2 that binds productively to MHC class II molecules initiating a T-cell response and/or the analogue is a conjugate comprising a polyhydroxypolymer backbone to which is separately coupled 1) the at least one foreign T_H epitope and 2) a disrupted sequence of APP or Aβ so that the analogue does not include any subsequence of SEQ ID NO: 2 that binds productively to MHC class II molecules initiating a T-cell response, wherein the polyamino acid and T_H epitope are attached to the polyhydroxypolymer by means of an amide bond.

25. The method according to claim 1, wherein the analogue is a conjugate comprising a polyhydroxypolymer backbone to which is separately coupled a polyamino acid that contains the at least one foreign T_H epitope and a disrupted APP or Aβ sequence so that the analogue does not include any subsequence of SEQ ID NO: 2 that binds productively to MHC class II molecules initiating a T-cell response, and/or the analogue is a conjugate comprising a polyhydroxypolymer backbone to which is separately coupled 1) the at least one foreign T_H epitope and 2) a disrupted sequence of APP or Aβ so that the analogue does not include any subsequence of SEQ ID NO: 2 that binds productively to MHC class II molecules initiating a T-cell response, wherein the polyhydroxypolymer is a polysaccharide.

26. The method according to claim 1, wherein the analogue has been formulated with an adjuvant which facilitates breaking of autotolerance to autoantigens.

27. The method according to claim 1, wherein an effective amount of the analogue is administered to the animal via a route selected from the parenteral route; the peritoneal route; the oral route; the buccal route; the sublinqual route;

the epidural route; the spinal route; the anal route; and the intracranial route.

28. The method of claim 27, wherein the parenteral route is selected from the intracutaneous, the subcutaneous, and the intramuscular routes.

29. The method according to claim 27, wherein the effective amount is between 0.5 μg and 2,000 μg of the analogue.

30. The method according to claim 1, wherein the analogue is a polyamino acid that contains the at least one foreign T_H epitope and a disrupted APP or Aβ sequence so that the analogue does not include any subsequence of SEQ ID NO: 2 that binds productively to MHC class II molecules initiating a T-cell response, wherein presentation of the analogue to the immune system is effected by introducing nucleic acid(s) encoding the analogue into the animal's cells and thereby obtaining *in vivo* expression by the cells of the nucleic acid(s) introduced.

31. The method according to claim 30, wherein the nucleic acid(s) introduced is/are selected from naked DNA, DNA formulated with charged or uncharged lipids, DNA formulated in liposomes, DNA included in a viral vector, DNA formulated with a transfection-facilitating protein or polypeptide, DNA formulated with a targeting protein or polypeptide, DNA formulated with Calcium precipitating agents, DNA coupled to an inert carrier molecule, DNA encapsulated in chitin or chitosan, and DNA formulated with an adjuvant.

32. The method according to claim 27, wherein the analogue is administered at a frequency of at least one administration/introduction per year.

33. The method according to claim 32, wherein the frequency of administration/introduction is selected from at least 2, at least 3, at least 4, at least 6, and at least 12 administrations/introductions.

34. The method according to claim 1 used for treating and/or preventing and/or ameliorating Alzheimer's disease or other diseases and conditions characterized by amyloid deposits, where APP or Aβ is down-regulated to such an extent that the total amount of amyloid is decreased or that the rate of amyloid formation is reduced with clinical significance.

35. An analogue of APP or Aβ which is derived from an animal APP or Aβ wherein is introduced a modification which has as a result that immunization of the animal with the analogue induces production of antibodies against the animal's autologous APP or Aβ, and wherein the analogue is as defined in claim 1.

36. An immunogenic composition comprising an immunogenically effective amount of an analogue according to claim 35, the composition further comprising a pharmaceutically and immunologically acceptable carrier and/or vehicle and optionally an adjuvant.

37. A nucleic acid fragment which encodes an analogue according to claim 35.

38. A vector carrying the nucleic acid fragment according to claim 37, such as a vector that is capable of autonomous replication.

39. The vector according to claim 38 which is selected from the group consisting of a plasmid, a phage, a cosmid, a mini-chromosome, and a virus.

40. The vector according to claim 38, comprising, in the 5'→3' direction and in operable linkage, a promoter for driving expression of the nucleic acid fragment which encodes an analogue of APP or Aβ which is derived from an animal APP or Aβ wherein is introduced a modification which has as a result that immunization of the animal with the analogue induces production of antibodies against the animal's autologous APP or Aβ, optionally a nucleic acid sequence encoding a leader peptide enabling secretion of or integration into the membrane of the polypeptide fragment, the nucleic acid fragment which encodes an analogue of APP or Aβ which is derived from an animal APP or Aβ wherein is introduced a modification which has as a result that immunization of the animal with the analogue induces production of antibodies against the animal's autologous APP or Aβ, and wherein the analogue is:

a) is a polyamino acid that contains the at least one foreign T_H epitope and a disrupted APP or Aβ sequence so that the analogue does not include any subsequence of SEQ ID NO: 2 that binds productively to MHC class II molecules initiating a T-cell response; and/or

b) is a conjugate comprising a polyhydroxypolymer backbone to which is separately coupled a polyamino acid as defined in a); and/or

c) is a conjugate comprising a polyhydroxypolymer backbone to which is separately coupled 1) the at least one

foreign T_H epitope and 2) a disrupted sequence of APP or Aβ as defined in a);

and optionally a terminator.

41. The vector according to claim 38 which, when introduced into a host cell, is capable or incapable of being integrated in the host cell genome.

42. The vector according to claim 40, wherein the promoter drives expression in a eukaryotic cell and/or in a prokaryotic cell.

43. A transformed cell carrying the vector of claim 38.

44. The transformed cell of claim 43, wherein the transformed cell is capable of replicating a nucleic acid fragment which encodes an analogue of APP or Aβ which is derived from an animal APP or Aβ wherein is introduced a modification which has as a result that immunization of the animal with the analogue induces production of antibodies against the animal's autologous APP or Aβ.

45. The transformed cell according to claim 43, which is a microorganism selected from a bacterium, a yeast, a protozoan, or a cell derived from a multicellular organism selected from a fungus, an insect cell, a plant cell, and a mammalian cell.

46. The transformed cell of claim 45, wherein the insect cell is selected from an S_2 and an SF cell.

47. The transformed cell according to claim 43, which expresses nucleic acid fragment which encodes an analogue of APP or Aβ which is derived from an animal APP or Aβ wherein is

introduced a modification which has as a result that immunization of the animal with the analogue induces production of antibodies against the animal's autologous APP or Aβ.

48. The transformed cell according to claim 43, wherein the transformed cell secretes or carries on its surface an analogue of APP or Aβ which is derived from an animal APP or Aβ wherein is introduced a modification which has as a result that immunization of the animal with the analogue induces production of antibodies against the animal's autologous APP or Aβ.

49. The method according to claim 1, wherein the analogue is a polyamino acid that contains the at least one foreign T_H epitope and a disrupted APP or Aβ sequence so that the analogue does not include any subsequence of SEQ ID NO: 2 that binds productively to MHC class II molecules initiating a T-cell response, wherein presentation to the immune system is effected by administering a non-pathogenic microorganism or virus which is carrying a nucleic acid fragment which encodes and expresses the analogue.

50. A composition for inducing production of antibodies against amyloid, the composition comprising

- a nucleic acid fragment which encodes an analogue of APP or Aβ which is derived from an animal APP or Aβ wherein is introduced a modification which has as a result that immunization of the animal with the analogue induces production of antibodies against the animal's autologous APP or Aβ or a vector according to claim 27, and

- a pharmaceutically and immunologically acceptable carrier and/or vehicle and/or adjuvant.

51. A stable cell line which carries the vector carrying a nucleic acid fragment which encodes an analogue according to claim 35, such as a vector that is capable of autonomous replication and which expresses the nucleic acid fragment which encodes an analogue according to claim 35, and which optionally secretes or carries the analogue according to claim 35 on its surface.